CLINICAL CONCEPTS AND COMMENTARY

Richard B. Weiskopf, M.D., Editor

The following correspondence refers to a previously published Clinical Concepts and Commentary article by Stephen E. Abram (Treatment of lumbosacral radiculopathy with epidural steroids. ANESTHESIOLOGY 1999; 91:1937–41).

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An Additional Dimension to the Efficacy of Epidural Steroids

To the Editor:—I enjoyed the article by Dr. Stephen Abram.[1] I would like to point out that an additional dimension to the discussion of effectiveness of epidural steroids can be found by applying the "numbers needed to treat" approach, as outlined in the excellent resource regarding the topic of pain relief using an evidence-based medicine approach published recently by McQuay and Moore.[2]

An additional important potential complication of administration of Depo corticosteroids has come to my attention, and I believe that it should be mentioned, particularly with reference to Depo-Medrol (Pharmacia & Upjohn, Peapack, NJ). Inadvertent intravascular administration of Depo corticosteroid, producing occlusion of small end arteries, was reported to result in visual defects in one case.[3] I am aware of a further case that involved a suboccipital nerve block, and the patient experienced ongoing hearing loss. Both of these cases were associated with administration of Depo corticosteroid in the head and neck area, with the potential for retrograde flow into end arteries. The risk of Depo corticosteroid reaching end arteries from epidural administration will presumably be smaller, although one must have some concern about particulate matter reaching small radicles of spinal arteries.

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Need for Precise Diagnosis prior to Epidural Steroids

To the Editor:—It was indeed reassuring to read the objective commentary of the application of epidural steroids by Abram,[1] which provided a brief but explicit review of the subject. I would like to point out that symptoms of radiculopathy may be caused by tumors, infections, vascular malformations, neuropathy spinal stenosis, facet joint arthropathy, a bulging disc in a patient with short pedicles, and by other diagnoses in a nonoperated spine. Postlaminectomy radiculopathy may occur, for example, from periroot scarring, a loose fragment of the herniated disc, arachnoiditis, or osteophytes. Even if we know that there is a herniated nucleus pulopsus, unless we define that the herniation of the disc is central, paracentral, or lateral, or that it is 2, 3, or 4 mm and that it is effacing the dural sac or compressing the root, we do not know whether epidural steroids are indicated. We do not claim originality regarding this concern; in 1944, Rovenstine and Hershey[2] stated that "Much discredit has come to nerve blocking from the too frequent practice of 'trying a block' without accurate diagnosis."

The diagram shown in figure 1 of Abram's article[1] illustrates a lateral herniated nucleus pulposus compressing the root against the posterior wall of the laminae; this is one of the situations in which epidural steroids have less chance to succeed, and it is precisely a situation that will most likely necessitate surgery. Usually when there is a space-occupying lesion, the epidural space is reduced or absent, and therefore attempts to enter the space at the same level have greater chances for dural puncture.

Two preparations mentioned by Abram,[1] Aristocort Forte (triamcinolone; ESI Lederle Generics, Philadelphia, PA) and Depo-Medrol (methylpredisolone; Pharmacia & Upjohn, Kalamazoo, MI), in multiple-dose

vials (5 ml), contain benzylic alcohol, in addition to polyethyleme glycol, both of which have been shown to be neurotoxic and should therefore be avoided.

Abram[3] noted no untoward effects from subarachnoid injections of methylprednisolone in 37 patients with sciatica. Kikuchi *et al.*[4] successfully treated patients with persistent pain from postherpetic neuralgia with use of subarachnoid injections of methylprednisolone. Our experience with intrathecal methylprednisolone administered after removal of the supernatant fluid and dilution of the remnants with iced saline has continued to provide satisfactory analgesia, without evidence of neurotoxicity (as indicated by neurologic examination and annual magnetic resonance imaging studies).[5,6] Abram *et al.*[7] administered four intrathecal steroid injections into rats at 3-week intervals without finding histologic abnormalities postmortem. We believe that limited observations should be continued to explore further the indications, safety, and effectiveness of intrathecal steroids, because extradural disease cannot be treated by intrathecal steroids,[3] and intrathecal disease cannot be treated by peridural steroids.

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In Reply:—Dr. Cousins and Drs. Aldrete and Ghaly raise several important issues. I agree with Dr. Cousins's suggestion about using the "numbers needed to treat" approach as a statistical tool to assess outcomes after epidural steroid injections. The problem remains that many of the existing studies in which such an approach could be applied are methodologically flawed.[1] Recent efforts to organize a large, methodologically sound, randomized study have been unsuccessful. One such project was organized through the Pain Outcomes Research Group of the American Society of Regional Anesthesia and Pain Medicine, Richmond, Virginia. The principal reason for the failure of that project was that referring surgeons were reluctant to enroll their patients into such studies because they were convinced of the effectiveness of epidural steroid injections and did not wish to delay effective therapy for those patients who would serve as controls. Perhaps such a study could be organized in a country in which the use of epidural steroid injections is not as widely accepted.

I very much appreciate Dr. Cousins's comments about the potential for harm from occlusion of small-end arteries by steroid suspensions. Methylprednisolone acetate tends to form aggregates of the steroid material when mixed with local anesthetic and may pose more of a risk for this problem than methylprednisolone acetate; but I suspect either preparation could produce devastating consequences if injected into a spinal artery. An animal model for this type of injury could possibly be developed.

I agree with the comments of Drs. Aldrete and Ghaly that it would be ideal to have a definitive diagnosis before initiation of epidural steroid injections. For patients who underwent previous spine surgery or who have a complicated or atypical medical history, imaging studies should certainly be performed before an injection. However, we often see patients whose history and physical findings are very typical of disk herniation and radiculopathy and who appear to be ideal epidural steroid candidates. In that situation, the principle reason to perform magnetic resonance imaging is to rule out a rare alternate cause of symptoms because there is poor correlation between imaging results and response to epidural steroids.[2] Is it worth performing a $1,500.00 study to rule out a condition with an incidence of 1 in 10,000 or 1 in 100,000? I am aware of only one case in which bleeding occurred after an epidural steroid injection in a patient with an intraspinal tumor. In that case, the lesion was misdiagnosed after myelography as disc herniation.

I disagree with Aldrete and Ghaly's comments about the diagram in figure 1. Their statement that the condition illustrated (mechanical compression of the nerve root) is likely to end up in surgery is probably true. However, Pawl[3] studied the effects of epidural steroid injections among patients who had been preselected as surgical candidates and who had signs of nerve root compression. He found that 50% of patients with cervical radiculopathy and 35% of patients with lumbar radiculopathy sufficiently benefitted from epidural steroids to avoid surgery.

The statement by Aldrete and Ghaly that dural puncture is more

likely to occur if injection is done at the level of disc herniation is unfounded. As shown by Hogan,[4] there is a segmentally occurring pyramidal space occupied by epidural fat that lies beneath the ligamanta flava. This rather generous space, into which the needle passes during a midline approach, would not be distorted by disc herniation. Most authors, including myself, recommend injecting the steroid as closely as possible to the level of the affected nerve root.

Aldrete and Ghaly state that triamcinolone diacetate (Aristocort Forte and Aristocort Intralesional; Fujisawa, Deerfield, IL) and methylprednisolone acetate (Depo-Medrol; Pharmacia & Upjohn, Bridgewater, NJ) contain benzyl alcohol and polyethylene glycol, both of which are neurotoxic. I know of no study that has shown neurotoxicity of these preparations or of the components of the vehicle in the concentrations found in the commercial preparations. As Drs. Aldrete and Ghaly point out subsequently, both of these preparations have been shown to be devoid of adverse effects when administered intrathecally or epidurally in animals.[5,6]

Unlike Aldrete and Ghaly, I would continue to urge caution when considering intrathecal injections of corticosteroids. My series of intrathecal steroid injections[7] was not devoid of adverse effects, as these authors suggested. There were several patients in whom transient symptoms developed compatible with a diagnosis of aseptic meningitis. Although I do not believe there is a high risk for the development of arachnoiditis, the literature regarding the use of repeated epidural steroid injections in patients with multiple sclerosis raises some concerns.

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